REMARKS

This amendment is responsive to the Final Rejection dated May 7, 2003. Claims 1-5, 10, 13-16 and 18 are amended herein. Claims 1-20 will be pending in the present application upon entry of this amendment.

Claims 1-3, 5, 13-16 and 18 have been amended to replace, "one or more compounds effective to regulate at least one of cell differentiation and cell proliferation," with "one or more compounds effective to inhibit at least one of cell differentiation and cell proliferation." Basis for this amendment is found at page 4, lines 14-22 of the specification as originally filed.

Claim 4 has been amended to delete the phrase, "structurally similar derivatives thereof which exhibit antioxidant activity." Claim 10 has been amended to delete the reference to "compounds containing selenium."

Entry of the amendments is requested on the basis that these amendments place the application in condition for allowance, or, on the basis that these amendments place the application in better form for appeal.

Information Disclosure Statement

Applicant would like to clarify its previous request that each item cited in the Information Disclosure Statement (IDS) dated March 19, 2002, be considered in the examination of the present application. Applicant notes that, under 37 C.F.R. § 1.98(a)(1), an IDS may include "patents, publications, applications, or **other information** submitted for consideration by the Office ..." [*Emphasis added.*] Since the downloaded items do not contain sufficient information to meet the requirements for consideration as a publication, as the Examiner has correctly pointed out, the rule provides that they can nevertheless be considered as "other information." The only requirements appearing in 37 C.F.R. § 1.98 for consideration of "other information" by the Examiner is that the other information must be listed in the IDS and a legible copy must be submitted with the IDS. This Applicant has done. The Examiner's consideration of the downloaded items is therefore earnestly solicited.

It is noted that in the Final Rejection dated May 7, 2003, the Examiner relied on the following quotation from 37 C.F.R. 1.98 in support of the Examiner's position that the "other information" cited in applicant's IDS need not be considered,

> Each publication listed in an information disclosure statement must be identified by publisher, author (if any), title, relevant pages of the publication, date, and place of publication." (emphasis added)

To clarify the applicant's position, the items lined through by the Examiner and not yet considered are not publications, but rather are, "other information." Thus, the passage of 37 C.F.R. 1.98 relied on by the Examiner and quoted above, does not apply since this passage only applies to publications, but does not mention "other information."

37 C.F.R. 1.98 also provides that,

> (a) Any information disclosure statement filed under §1.97 shall include:
> (1) A list of all patents, publications, applications, or other information submitted for consideration by the Office;
> (2) A legible copy of:...
> (iv) All other information or that portion which caused it to be listed;...

Thus, from this quotation it is clear that:

(1) "Other information" is something different from "publications" since it is listed separately in 37 C.F.R. §1.98(a)(1).

(2) The only requirements in an IDS for consideration of "other information," that is in the English language (as is all of the "other information cited herein), are that the other information be listed in the IDS and that the applicant must provide a legible copy of the "other information."

Accordingly, since the applicant has listed the "other information" in the IDS and has provided a legible copy of the "other information," it is clear that the applicant has complied with all of the requirements of 37 C.F.R. 1.98 for consideration of this information. Therefore, the Examiner is requested to consider this "other information." In this connection, Applicant would not object if the consideration of the "other information" were recorded in an Official Action rather than a Form PTO-1449. Similarly, Applicant would not object if the Examiner chose not to list the "other information" on the face of any patent that might issue based on the present application, so long as the record reflects that this information has been considered by the Examiner.

Rejections under 35 U.S.C. § 112

Claims 1-20 have been rejected under 35 U.S.C. § 112, first paragraph, on the basis that the instant specification fails to provide adequate support for the claimed compositions in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the invention. This rejection, at least insofar as it applies to claims 1-20, as amended, is respectfully traversed and reconsideration is requested for the reasons which follow.

The Case of *Regents of the University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (CAFC 1997)

The Examiner relies on the following statements from the case of *Regents of the University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (CAFC 1997) (hereinafter, "*Eli Lilly*")[1] in support of the rejection,

> [A] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials...
>
> It does not define any structural features commonly possessed by members of the genus that distinguish from others. One skilled in the art therefore, cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus.

Eli Lilly at 1405. Although these statements appear in *Eli Lilly*, further investigation clearly demonstrates that these statements are not the applicable law. The reason for this is that the statements from *Eli Lilly* quoted above are *Obiter dictum* and therefore are not binding precedent.

More specifically, *Black's Law Dictionary, Fifth Edition,* p. 967 (copy enclosed), defines *Obiter dictum* as "Words of an opinion entirely unnecessary for the decision of the case." *Black's Law Dictionary, Fifth Edition*, p. 967, also states that *Obiter dictum* are not binding as precedent.

[1] The applicant has enclosed copies of all of the cases cited herein for the convenience of the Examiner since the applicant did not have ready access to the USPQ2d version of the cases and thus had to provide jump cites only for the F.3d versions. The enclosed copies of the cases include the F.3d page numbers in brackets preceded by an asterisk so that the Examiner can find the quotations relied on herein by the applicant.

The relevant issues before the Court of Appeals for the Federal Circuit (hereinafter "CAFC") in *Eli Lilly* were whether the specification enabled claims requiring one of:

(a) cDNA encoding human insulin,

(b) cDNA encoding vertebrate insulin, and

(c) cDNA encoding mammalian insulin.

See *Eli Lilly* at 1567. Thus, any statement in *Eli Lilly* relating to a chemical genus or a chemical species, such as those quoted by the Examiner, are *Obiter dictum* because it was entirely unnecessary for the CAFC to consider a chemical genus or a chemical species in order to decide whether the specification enabled claims to cDNA, since cDNA is not a chemical species or genus. Accordingly, since these statements are *Obiter dictum*, they are not binding precedent and therefore do not represent the applicable law.

The actual holding of *Eli Lilly* that is binding legal precedent is, at most, that an adequate written description of cDNA that encodes human, vertebrate or mammalian insulin requires a precise definition, such as by structure, formula, chemical name or physical properties, sufficient to distinguish it from other materials, or if the disclosed function is sufficiently correlated to a particular, known structure. This was confirmed by the CAFC itself when it said,

> More recently, in *Enzo Biochem* [*v. Gen-Probe, Inc.*, 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002)], we clarified that *Eli Lilly* did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if, in the knowledge of the art, the disclosed function is sufficiently correlated to a particular, known structure.

Amgen Inc. v. Hoechst Marion Roussel Inc., 314 F.3d 1313, 1332, 65 USPQ2d 1385, 1399 (Fed. Cir. 2003).

Also,

> The language of § 112, ¶ 1 indicates that a patent will contain an adequate description if it provides enough information to enable a person skilled in the art to make and use the invention. Any disclosure that enables one to make and use the invention also, by definition, also shows that the inventor was in possession of that full invention. Consequently, the erroneous written description requirement of [the] *Lilly* case lacks both a statutory and a logical foundation. (Emphasis added)

Moba, B.V., et al. v. Diamond Automation, Inc., 325 F.3d 1306, 1323, 66 USPQ2d 1429 (Fed. Cir. 2003) (Rader, J., concurring). The emphasized portion of this quotation confirms that even the Federal Circuit has admitted that the written description requirement of *Eli Lilly* is erroneous.

The correct interpretation of the written description requirement of 35 U.S.C. 112, first paragraph, can be found in *Enzo Biochem v. Gen-Probe, Inc.*, 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002) (hereinafter, "*Enzo Biochem*"). In relevant part, *Enzo Biochem* held that,

> It is not correct, however, that all functional descriptions of genetic material fail to meet the written description requirement. The PTO has issued Guidelines governing its internal practice of addressing that issue... In its Guidelines, the PTO has determined that the written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics... i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." Guidelines, *66 Fed. Reg. at 1106.* ...**We are persuaded by the Guidelines on this point and adopt the PTO's applicable standard for determining compliance with the written description requirement.** (emphasis added)

Enzo Biochem, 296 F.3d at 1324. Thus, in view of this CAFC decision, the issue of whether the present specification meets the written description requirement of 35 U.S.C. 112, first paragraph, should be decided on the basis of the U.S. Patent and Trademark Office's Written Description Guidelines, and not on the basis of the above-quoted statement of *Obiter dictum* from *Eli Lilly*, which even the CAFC itself has acknowledged is incorrect.

Even the MPEP does not apply the *Eli Lilly* case to a chemical genus or species. Rather, the MPEP characterizes the holding of *Eli Lilly* as limited to a "coding sequence" (i.e. cDNA) when it states,

> A definition by function alone "does not suffice" to sufficiently describe a **coding sequence** "because it is only an indication of what the gene does, rather than what it is." *Eli Lilly*, 110 F.3[d] at 1568, 43 USPQ2d at 1406.

See MPEP §2162, II.A.2, p. 2100-166.

Finally, it is well-established that functional language may be used to describe and claim a component of a composition. In fact, the M.P.E.P. at § 2173(g) sets forth the following example of functional language that has been used appropriately in a similar context:

> It was held that the limitation used to define a radical on a chemical compound as "incapable of forming a dye with said oxidizing developing agent" although functional, was perfectly acceptable because it set definite boundaries on the patent protection sought. [*Citation omitted.*]

The USPTO Written Description Guidelines

According to the USPTO Written Description Guidelines, there are at least two ways that the specification of the present application can satisfy the requirements of 35 U.S.C. 112, first paragraph. First,

> The written description requirement can be met by 'showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics... i.e. complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.'"

Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶1, "Written Description" Requirement, 66 Fed.Reg. 1099, 1166 (Jan. 5, 2001).

Second,

> [The written description requirement] may be satisfied through sufficient description of a representative number of species by actual reduction to practice, ..."

MPEP §2163, II,A.3(a)(ii) and *Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶1, "Written Description" Requirement, 66 Fed.Reg. 1099, 1106 (Jan. 5, 2001).*

The U.S. Patent and Trademark Office Written Description Guidelines also provide that,

> A 'representative number of species' means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. On the other hand, there may be situations where one species adequately supports a genus. What constitutes a 'representative number' is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a 'representative number' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. Description of a representative number of species does not require the

> description to be of such specificity that it would provide individual support for each species that the genus embraces.

Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶1, "Written Description" Requirement, 66 Fed.Reg. 1099, 1106 (Jan. 5, 2001).

The applicant will demonstrate below that one or both of these requirements is satisfied by the present application for each term objected to by the Examiner, and that the present application contains significantly more disclosure for most of these terms than is contained in issued U.S. Patents which employ the same terminology in their claims.

The Rejections Under 35 U.S.C. §112, First Paragraph

A. One or More Compounds Effective to Inhibit at Least One of Cell Differentiation and Cell Proliferation."

Claims 1-20 have been rejected under 35 U.SC. § 112, first paragraph, due to the inclusion of the term "one or more compounds effective to regulate at least one of cell differentiation and cell proliferation." This rejection, at least insofar as it applies to claims 1-20, as amended, is respectfully traversed and reconsideration is requested for the reasons which follow.

The applicant has amended claims 1-20 to replace the term, "regulate" with the term, "inhibit" to more particularly specify this aspect of the invention. This amendment conforms the claim language to the tests that are well-known to persons of skill in the art for determining whether a particular compound inhibits cell differentiation or cell proliferation and eliminates potential ambiguities created by use of the term, "regulate."

As demonstrated above, the Examiner's sole basis for this rejection, the quoted statements from *Eli Lilly*, are not the applicable law, and thus the Examiner's rejection must be reviewed in light of the U.S. Patent Office Written Description Guidelines, which are the applicable law for the present case. For this purpose, the applicant encloses herewith a Declaration under 37 C.F.R. §1.132 of Anthony William Addison, Professor of Chemistry at Drexel University in Philadelphia, PA (hereinafter, "the Addison Declaration"). Consideration and entry of the Addison Declaration is requested on the basis that it places the present application in condition for allowance, or, alternatively, on the basis that it places the present application in better form for appeal.

Paragraphs 8-11 of the Addison Declaration demonstrate that the chemical genus, "one or more compounds effective to regulate at least one of cell differentiation and cell proliferation." meets the requirements of 35 U.S.C. 112, first paragraph, since:

(1) the specification of the present application discloses a representative number of species to support the genus,

(2) the level of knowledge and skill in the art is high,

(3) tests for determining whether a particular compound inhibits one or more of cell differentiation and cell proliferation are commercially available.

According to MPEP §2163, II.3.b:

> The examiner has the initial burden of presenting evidence or reasoning to explain why persons skilled in the art would not recognize in the original disclosure a description of the invention defined by the claims. See *Wertheim*, 541 F.2d at 263, 191 USPQ at 97 ("[T]he PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims.")

Although the Examiner initially presented reasoning based on the quoted statements from *Eli Lilly*, the applicant has demonstrated that this basis for the Examiner's rejection is not the applicable law, because the statements relied on by the Examiner from *Eli Lilly* are *Obiter dictum* and were acknowledged by the CAFC as being erroneous. As a result, since the Examiner's rationale in support of the rejection is not based on the applicable law, as demonstrated above, there is no longer any evidence or reasoning in the record upon which the Examiner's rejection can be based, and for this reason alone it should be withdrawn.

In addition, the applicant has now presented evidence in support of its position that the chemical genus, "one or more compounds effective to regulate at least one of cell differentiation and cell proliferation" meets the requirements of 35 U.S.C. 112, first paragraph, in the form of paragraphs 8-11 of the Addison Declaration. At present, this evidence is unrebutted. Accordingly, for this additional reason, the rejection should be withdrawn.

The Examiner also took the position that,

> The instant specification merely defines, for example, at page 4[,] line[s] 3-5, "The compound that regulates cell differentiation and/or cell proliferation that may be used in the composition of the present invention may be selected from suitable compounds that have this activity."

See page 4 of the Final Rejection. This statement, however, appears to be incorrect, as is demonstrated in paragraph 9 of the Addison Declaration, since the present application, as originally filed, contains several pages (pages 4-7 of the specification) of additional disclosure relating to the compounds that inhibit cell differentiation or cell proliferation. Thus, the disclosure of the present application goes far beyond the single quoted statement that the Examiner attributes to it and therefore satisfies the requirements of 35 U.S.C. 112, first paragraph for the reasons given in the Addison Declaration.

The Examiner also took the position that,

> One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. (emphasis original)

See page 4 of the Final Rejection. This statement also appears to be incorrect since, as paragraph 9 of the Addison Declaration points out, pages 4-7 of the original specification identify several members of the claimed genus. Thus, not only can the skilled person visualize or recognize the identity of members of the genus, the skilled person can do this by looking at the specification of the present application as originally filed, without having to look further.

The Examiner also took the position that,

> Claim 1 in particular reads on employment of any compounds effective to regulate at least one of cell differentiation and cell proliferation..., necessitating one of skill to perform an exhaustive search for the embodiments of any compounds having the activity herein suitable to practice the invention. (emphasis original)

See page 5 of the Final Rejection. The applicant disagrees that one of skill in the art needs to perform an exhaustive search for compounds meeting the requirements of claim 1 in order to practice the invention. Rather, a skilled person desiring to practice the invention need only look to the specification and select one of the several species of compounds that inhibit cell differentiation or cell proliferation disclosed therein at pages 4-7, in order to practice the invention. No searching for compounds is necessary at all.

Moreover, if a skilled person would like to determine whether a particular compound not mentioned in the specification of the present application meets the language of claim 1, the skilled person need only subject that compound to a routine test, such as that commercially available from DiscoverRx, to determine if that compound inhibits cell differentiation or cell

proliferation. These facts are very similar to the example of reasonable experimentation found at MPEP §2164.06(I), which reads,

> In *United States v. Telectronics, Inc.*, 857 F.2d 778, 8 USPQ2d 1217 (Fed. Cir. 1988), *cert. denied*, 490 U.S. 1046 (1989), the court reversed the findings of the district court for lack of clear and convincing proof that undue experimentation was needed. The court ruled that since one embodiment (stainless steel electrodes) and the method to determine the dose/response was set forth in the specification, the specification was enabling. The question of time and expense of such studies, approximately $50,000 and 6-12 months standing alone, failed to show undue experimentation.

In the present case, there are several embodiments disclosed at pages 4-7 of the specification and methods to determine whether a compound inhibits cell differentiation or cell proliferation (e.g. the DiscoverRx test) were well known to persons skilled in the art and commercially available. These methods are also significantly less expensive and time-consuming than the methods of the above-cited example. Thus, the rejection should be withdrawn.

Finally, the Examiner states at page 6 of the Final Rejection that a patent is not a hunting license, it is compensation for the successful conclusion of a search. In the present case, the applicant has performed this search and has specifically identified several working embodiments of compounds that inhibit cell proliferation or cell differentiation at pages 4-7 of the application as originally filed. Under the patent laws, it is clear that the applicant is entitled to protection for more than the exact, specifically identified embodiments of the invention which are listed in the specification. In the present case, the applicant is merely employing claim language that provides adequate coverage for the invention since, if the applicant were to limit the claims to the specific embodiments disclosed in the specification, third parties would be able to easily appropriate the applicant's invention by identifying an undisclosed compound that inhibits cell differentiation or cell proliferation, using the routine tests that are commercially available, and substituting that compound into the composition. As a result, the applicant's patent protection would potentially be rendered worthless through the exercise of routine, non-inventive, experimentation by a third party. This is certainly not the intention of the patent system.

Accordingly, for the foregoing reasons, withdrawal of the rejection of claims 1-20 under 35 U.S.C. 112, first paragraph, on the basis of the language, "one or more compounds effective to regulate at least one of cell differentiation and cell proliferation" is respectfully requested.

B. The Terminology, "One or More Antioxidants"

Claims 1-20 have been rejected under 35 U.SC. § 112, first paragraph, due to the inclusion of the term "one or more antioxidants." This rejection, at least insofar as it applies to claims 1-20, as amended, is respectfully traversed and reconsideration is requested for the reasons which follow.

The same arguments given above with respect to the *Eli Lilly* case also apply here. In addition, paragraphs 12-21 of the Addison Declaration provide detailed facts and evidence which clearly demonstrate that the terminology, "one or more antioxidants" meets the requirements of 35 U.S.C. 112, first paragraph, in the context of the present application. More specifically, the Addison Declaration presents four independent, convincing reasons why the terminology, "one or more antioxidants" should be accepted:

(1) Page 7 of the specification as originally filed discloses a representative number of species of antioxidants sufficient to support the claimed genus, as supported by detailed facts and evidence given in paragraphs 14 and 16 of the Addison Declaration.

(2) The functional definition "antioxidants," coupled with the known correlations between antioxidant activity and chemical structure, is sufficient to meet the test of *Enzo Biochem*, as supported by detailed facts and evidence given in paragraphs 16-17 of the Addison Declaration.

(3) The fact that at least 5281 U.S. Patents have issued since 1976 using the terms, "antioxidant" or "antioxidants" in the claims of the patent.

(4) The fact that the present application contains substantially more disclosure relative to "antioxidants" than issued U.S. Patent no. 5,747,026, which claims "antioxidants," and which U.S. patent is presumed to meet the requirements of 35 U.S.C. 112, first paragraph, since it is an examined, issued patent. See 35 U.S.C. 282 and paragraphs 18-21 of the Addison Declaration.

In addition, the same arguments given above with respect to the language, "compounds that inhibit one or more of cell differentiation and cell proliferation" also apply to the language "one or more antioxidants."

Accordingly, for these reasons the rejection of claims 1-20 based on the terminology, "one or more antioxidants" should be withdrawn.

C. The Terminology "Structurally Similar Derivatives Thereof Which Exhibit Antioxidant Activity"

Claim 4 has been rejected under 35 U.S.C. §112, first paragraph, on the basis that it contains the phrase, "structurally similar derivatives thereof which exhibit antioxidant activity." Although the applicant does not agree that the Examiner's position is correct, by this amendment, this phrase has been deleted from claim 4 in order to obviate the rejection. Favorable consideration and withdrawal of the rejection in view of this amendment is requested.

D. The Terminology "One or More Antioxidant Enzymes"

Claim 6 has been rejected under 35 U.SC. § 112, first paragraph, due to the inclusion of the term "one or more antioxidant enzymes." This rejection, at least insofar as it applies to claim 6, as amended, is respectfully traversed and reconsideration is requested for the reasons which follow.

The same arguments given above with respect to the *Eli Lilly* case also apply here. In addition, paragraphs 22-30 of the Addison Declaration provide detailed facts and evidence which clearly demonstrate that the terminology, "one or more antioxidant enzymes" meets the requirements of 35 U.S.C. 112, first paragraph, in the context of the present application. More specifically, the Addison Declaration presents three independent, convincing reasons why the terminology, "one or more antioxidant enzymes" should be accepted:

(1) Page 8, lines 4-6 of the specification as originally filed discloses a representative number of species of antioxidant enzymes sufficient to support the claimed genus, as supported by detailed facts and evidence given in paragraphs 24 and 26 of the Addison Declaration.

(2) The fact that the present application contains substantially more disclosure relative to "antioxidant enzymes" than issued U.S. Patent no. 5,747,026, which claims

"antioxidant enzymes" and which U.S. patent is presumed to meet the requirements of 35 U.S.C. 112, first paragraph, since it is an examined, issued patent. See 35 U.S.C. 282 and paragraphs 28-30 of the Addison Declaration.

(3) The disclosure of the several species of antioxidant enzymes in the original application, taken together with the known assays for antioxidant enzymes and the known antioxidant enzymes themselves, are sufficient to demonstrate that the applicant had possession of the invention, as supported by detailed facts and evidence given in paragraphs 24-26 of the Addison Declaration.

In addition, the same arguments given above with respect to the language, "one or more compounds effective to regulate at least one of cell differentiation and cell proliferation" also apply to the language "one or more antioxidant enzymes."

Accordingly, for these reasons the rejection of claim 6 based on the terminology, "one or more antioxidant enzymes" should be withdrawn.

E. The Terminology "Anti-Inflammatories"

Claim 12 has been rejected under 35 U.SC. § 112, first paragraph, due to the inclusion of the term "anti-inflammatories" This rejection, at least insofar as it applies to claim 12, as amended, is respectfully traversed and reconsideration is requested for the reasons which follow.

The same arguments given above with respect to the *Eli Lilly* case also apply here. In addition, paragraphs 31-41 of the Addison Declaration provide detailed facts and evidence which clearly demonstrate that the terminology, "anti-inflammatories" meets the requirements of 35 U.S.C. 112, first paragraph, in the context of the present application. More specifically, the Addison Declaration presents four independent, convincing reasons why the terminology, "anti-inflammatories" should be accepted:

(1) At least 2936 U.S. Patents have been issued since 1976 containing the word, "anti-inflammatory" in the claims of the patent and at least 186 U.S. patents have been issued since 1976 containing the word, "anti-inflammatories" in the claims of the patent.

(2) The specification as originally filed disclosed a species of anti-inflammatory and the FDA maintains a list of approved anti-inflammatories, and thus the various species of anti-inflammatories disclosed in the specification or well known to skilled persons is

sufficient to support the claimed genus, as supported by detailed facts and evidence given in paragraphs 31, 33 and 35 the Addison Declaration.

(3) The functional definition "anti-inflammatory," coupled with the known correlations between anti-inflammatory activity and chemical structure, is sufficient to meet the test of *Enzo Biochem*, as supported by detailed facts and evidence given in paragraphs 36-37 of the Addison Declaration.

(4) The fact that the present application contains at least the same amount of disclosure relative to "anti-inflammatories" as issued U.S. Patent no. 6,465,003 B2, which claims "anti-inflammatories" and is presumed to meet the requirements of 35 U.S.C. 112, first paragraph, since it is an examined, issued patent. See 35 U.S.C. 282 and paragraphs 38-41 of the Addison Declaration.

In addition, the same arguments given above with respect to the language, "one or more compounds effective to regulate at least one of cell differentiation and cell proliferation," also apply to the language "anti-inflammatories"

Accordingly, for these reasons the rejection of claim 12, based on the terminology, "anti-inflammatories" should be withdrawn.

The Rejections Under 35 U.S.C. §112, Second Paragraph

A. The Terminology "One or More Compounds Effective to Inhibit at Least One of Cell Differentiation and Cell Proliferation"

Claims 1-20 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite on the basis that these claims include the terminology, "one or more compounds effective to inhibit at least one of cell differentiation and cell proliferation."

As stated in the M.P.E.P. at § 2173.02,

> The essential inquiry pertaining to this requirement is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity. Definiteness of claim language must be analyzed, not in a vacuum, but in light of:
>
> (A) The content of the particular application disclosure;
>
> (B) The teachings of the prior art; and

> (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.

An extensive discussion of "one or more compounds effective to inhibit at least one of cell differentiation and cell proliferation." can be found in the specification at pages 4-7. Thus, those of skill in the art can readily ascertain whether or not a given compound possesses the requisite activity and, consequently, whether or not the compound is suitable for use in the claimed invention.

According to MPEP §2173.02,

> If the language of the claim is such that a person of ordinary skill in the art could not interpret the metes and bounds of the claim so as to understand how to avoid infringement, a rejection of the claim under 35 U.S.C. 112, second paragraph, would be appropriate. See *Morton Int'l, Inc. v. Cardinal Chem. Co.*, 5 F.3d 1464, 1470, 28 USPQ2d 1190, 1195 (Fed. Cir. 1993) (hereinafter "*Morton*").

Also, according to MPEP §2173.05(g) regarding functional limitations,

> It was held that the limitation used to define a radical on a chemical compound as "incapable of forming a dye with said oxidizing developing agent" although functional, was perfectly acceptable because it set definite boundaries on the patent protection sought. *In re Barr*, 444 F.2d 588, 170 USPQ 33 (CCPA 1971).

Thus, the question is whether the terminology, "one or more compounds effective to inhibit at least one of cell differentiation and cell proliferation" sets definite boundaries on the patent protection sought. The only reason given by the Examiner in support of this rejection is that one of ordinary skill in the art could not interpret the metes and bounds of this language. However, the Examiner has not explained why this would be the case, nor has the Examiner offered any facts, evidence or arguments in support of this position.

The applicant, on the other hand, has shown that the specification discloses several species of these compounds and that there are well-known, commercially available tests for determining if a particular compound inhibits cell differentiation or cell proliferation. Thus, applying the test of *Morton*, the skilled person is easily able to understand how to avoid infringement. Specifically, the skilled person need only identify a compound, check to see if it is mentioned in the specification, if not, subject it to a simple test such as the DiscoverRx test and,

if it does not inhibit one of cell differentiation or cell proliferation, it avoids infringement. That is all there is to it.

Comparing this to the *In re Barr* case, there the skilled person also had to subject the radical to a simple test, i.e. expose it to the oxidizing developing agent, and determine if it formed a dye. Under these extremely similar circumstances, it was held that the claim terminology, though functional, met the requirements of 35 U.S.C. 112, second paragraph. The terminology, "one or more compounds effective to inhibit at least one of cell differentiation and/or cell proliferation." should be considered definite for the same reasons as are given in *In re Barr*.

The Examiner's remarks in response to the applicant's position on this issue found at page 6 of the Final Rejection are not understood since the only reasoning given by the Examiner is based on *Genentech*, 108 F.3d at 1366. However, the *Genentech* case related to the first paragraph of 35 U.S.C. 112 (i.e. enabling disclosure) and not to the second paragraph of 35 U.S.C. 112 (i.e. definiteness). Thus, the *Genentech* case is not relevant to whether the claims of the present application meet the requirements of the second paragraph of 35 U.S.C. 112.

Favorable consideration and withdrawal of the rejection are requested.

B. The Terminology "One or More Antioxidants"

Claims 1-20 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite on the basis that these claims include the terminology, "one or more antioxidants."

As stated in the M.P.E.P. at § 2173.02,

> The essential inquiry pertaining to this requirement is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity. Definiteness of claim language must be analyzed, not in a vacuum, but in light of:
>
> (A) The content of the particular application disclosure;
>
> (B) The teachings of the prior art; and
>
> (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.

Applicant respectfully submits that the term "one or more antioxidants" is sufficient to define the metes and bounds of the claims to those of skill in the art.

For example, paragraph 43 of the Addison Declaration concludes that the skilled person is able to determine the metes and bounds of the term, "one or more antioxidants" citing the following detailed facts and evidence in support thereof:

A. Since 1976, at least 5281 United States patents have been issued using the words "antioxidant" or "antioxidants" in the claims.

B. Numerous antioxidants are known to persons skilled in the art.

C. At least 25 different antioxidants are specifically listed in the '642 application.

D. Routine tests exist for determining whether a compound has antioxidant activity and thus a person of ordinary skill in the art can simply take a specific compound and test it for antioxidant activity to determine whether that compound falls within the metes and bounds of the claims.

E. In Professor Addison's experience, persons of ordinary skill in the art are capable of determining whether a particular chemical compound exhibits antioxidant activity and therefore is an antioxidant.

The question is whether the terminology, "one or more antioxidants" sets definite boundaries on the patent protection sought. The only reason given by the Examiner in support of this rejection is that one of ordinary skill in the art could not interpret the metes and bounds of this language. However, the Examiner has not explained why this would be the case, nor has the Examiner offered any facts, evidence or arguments in support of this position.

The applicant, on the other hand, has shown that the specification discloses numerous species of antioxidants, that there are well-known tests for determining if a particular compound exhibits antioxidant activity, and that in the experience of a skilled chemist, persons of ordinary skill in the art are capable of determining whether a particular compound is an antioxidant. Thus, applying the test of *Morton*, the skilled person is easily able to understand how to avoid infringement. Specifically, the skilled person need only identify a compound, check to see if it is listed in the present specification, if not, subject it to a simple test such as one of the several tests referenced in paragraph 43 of the Addison Declaration and, if it does not exhibit antioxidant activity, it avoids infringement. That is all there is to it.

Comparing this to the *In re Barr* case, there the skilled person also had to subject the radical to a simple test, i.e. expose it to the oxidizing developing agent, and determine if it formed a dye. Yet, under these extremely similar circumstances, it was held that the claim terminology, though functional, met the requirements of 35 U.S.C. 112, second paragraph. The terminology, "one or more antioxidants" should be considered definite for the same reasons as are given in *In re Barr*.

The Examiner's remarks in response to the applicant's position on this issue found at page 6 of the Final Rejection are not understood since the only reasoning given by the Examiner is based on *Genentech*, 108 F.3d at 1366. However, the *Genentech* case related to the first paragraph of 35 U.S.C. 112 (i.e. enabling disclosure) and not to the second paragraph of 35 U.S.C. 112 (i.e. definiteness). Thus, the *Genentech* case is not relevant to whether the claims of the present application meet the requirements of the second paragraph of 35 U.S.C. 112.

Finally, the U.S. Patent Office has issued at least 5281 U.S. Patents which contain the word, "antioxidant" or "antioxidants" in the claims. Each of these patents has been examined and is presumed valid pursuant to 35 U.S.C. 282. Thus, in at least 5281 patents, it was determined that the words, "antioxidant" or "antioxidants" was sufficiently definite to meet the requirements of 35 U.S.C. 112, second paragraph. The same conclusion should be reached in the present application.

Favorable consideration and withdrawal of the rejection are requested.

C. The Terminology "Structurally Similar Derivatives Thereof Which Exhibit Antioxidant Activity"

Claim 4 has been rejected under 35 U.S.C. §112, second paragraph, on the basis that it contains the phrase, "structurally similar derivatives thereof which exhibit antioxidant activity." Although the applicant does not agree that the Examiner's position is correct, by this amendment, this phrase has been deleted from claim 4 in order to obviate the rejection. Favorable consideration and withdrawal of the rejection in view of this amendment is requested.

D. The Terminology "One or More Antioxidant Enzymes"

Claim 6 has been rejected under 35 U.S.C. 112, second paragraph, as being indefinite on the basis that these claims include the terminology, "one or more antioxidant enzymes."

As stated in the M.P.E.P. at § 2173.02,

> The essential inquiry pertaining to this requirement is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity. Definiteness of claim language must be analyzed, not in a vacuum, but in light of:
>
> (A) The content of the particular application disclosure;
>
> (B) The teachings of the prior art; and
>
> (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.

Applicant respectfully submits that the term "one or more antioxidant enzymes" is sufficient to define the metes and bounds of the claims to those of skill in the art.

For example, paragraph 44 of the Addison Declaration concludes that the skilled person is able to determine the metes and bounds of the term, "one or more antioxidant enzymes" citing the following detailed facts and evidence in support thereof:

A. At least United States patent no. 5,747,026 has been issued claiming "antioxidant enzymes" in claim 2.
B. Several antioxidant enzymes are known to persons skilled in the art.
C. Several antioxidant enzymes are listed in the '642 application.
D. Routine assays exist for determining whether a chemical compound or an enzyme has antioxidant activity. Thus a person of ordinary skill in the art can simply take a specific enzyme and test it for antioxidant activity using a routine test to determine whether the compound falls within the metes and bounds of the claims.

The question is whether the terminology, "one or more antioxidant enzymes" sets definite boundaries on the patent protection sought. The only reason given by the Examiner in support of this rejection is that one of ordinary skill in the art could not interpret the metes and bounds of this language. However, the Examiner has not explained why this would be the case, nor has the Examiner offered any facts, evidence or arguments in support of this position.

The applicant, on the other hand, has shown that the specification discloses several species of these enzymes, that there are well-known tests for determining if a particular enzyme exhibits antioxidant activity, and that in the experience of a skilled chemist, persons of ordinary

skill in the art are capable of determining whether a particular enzyme is an antioxidant. Thus, applying the test of *Morton*, the skilled person is easily able to understand how to avoid infringement. Specifically, the skilled person need only identify an enzyme, check to see if it is listed in the specification, if not, subject it to a simple test such as one of the several tests referenced in paragraph 44 of the Addison Declaration and, if it does not exhibit antioxidant activity, it avoids infringement. That is all there is to it.

Comparing this to the *In re Barr* case, there the skilled person also had to subject the radical to a simple test, i.e. expose it to the oxidizing developing agent, and determine if it formed a dye. Under these extremely similar circumstances, it was held that the claim terminology, though functional, met the requirements of 35 U.S.C. 112, second paragraph. The terminology, "one or more antioxidant enzymes" should be considered definite for the same reasons as are given in *In re Barr.*

The Examiner's remarks in response to the applicant's position on this issue found at page 6 of the Final Rejection are not understood since the only reasoning given by the Examiner is based on *Genentech*, 108 F.3d at 1366. However, the *Genentech* case related to the first paragraph of 35 U.S.C. 112 (i.e. enabling disclosure) and not to the second paragraph of 35 U.S.C. 112 (i.e. definiteness). Thus, the *Genentech* case is not relevant to whether the claims of the present application meet the requirements of the second paragraph of 35 U.S.C. 112.

Finally, the U.S. Patent Office has issued at least U.S. Patent no. 5,747,026 which contains the phrase, "antioxidant enzymes" in the claims. This patent has been examined and is presumed valid pursuant to 35 U.S.C. 282. Thus, in at least U.S. Patent no. 5,747,026, it was determined that the phrase, "antioxidant enzymes" was sufficiently definite to meet the requirements of 35 U.S.C. 112, second paragraph. The same conclusion should be reached in the present application.

Favorable consideration and withdrawal of the rejection are requested.

E. The Terminology "Anti-Inflammatories"

Claim 12 has been rejected under 35 U.S.C. 112, second paragraph, as being indefinite on the basis that these claims include the terminology, "anti-inflammatories."

As stated in the M.P.E.P. at § 2173.02,

> The essential inquiry pertaining to this requirement is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity. Definiteness of claim language must be analyzed, not in a vacuum, but in light of:
>
> (A) The content of the particular application disclosure;
>
> (B) The teachings of the prior art; and
>
> (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.

Applicant respectfully submits that the term "anti-inflammatories" is sufficient to define the metes and bounds of the claims to those of skill in the art.

For example, paragraph 45 of the Addison Declaration concludes that the skilled person is able to determine the metes and bounds of the term, "anti-inflammatories" citing the following detailed facts and evidence in support thereof:

A. Since 1976, at least 3112 United States patents have been issued using the words "anti-inflammatory" or "anti-inflammatories" in the claims,
B. Numerous anti-inflammatories are known to persons skilled in the art,
C. Persons of ordinary skill in the art of chemistry are aware that there are known correlations between the function of a compound as an anti-inflammatory and the structure of a chemical compound.
D. The term, "anti-inflammatory" is a commonly used, well-known term in the art of chemistry as is evidenced by the fact that a definition of the term can be found on the FDA web site and that the term can be found in numerous dictionaries.

The question is whether the terminology, "anti-inflammatories" sets definite boundaries on the patent protection sought. The only reason given by the Examiner in support of this rejection is that one of ordinary skill in the art could not interpret the metes and bounds of this language. However, the Examiner has not explained why this would be the case, nor has the Examiner offered any facts, evidence or arguments in support of this position.

The applicant, on the other hand, has shown that the specification discloses a species of these compounds, that numerous anti-inflammatories are known from the FDA list of approved anti-inflammatories, that there are well-known tests for determining if a particular compound

exhibits anti-inflammatory activity (i.e. the FDA approves anti-inflammatories and, in this approval process, employs these well-known tests to determine if particular compounds have anti-inflammatory activity), and that persons of ordinary skill in the art are aware that there are known correlations between the function of a compound as an anti-inflammatory and the structure of a chemical compound. Thus, applying the test of *Morton*, the skilled person is easily able to understand how to avoid infringement. Specifically, the skilled person need only identify a compound, subject it to a simple test such as one of the tests applied by the FDA, and, if it does not exhibit anti-inflammatory activity, it avoids infringement. That is all there is to it.

Comparing this to the *In re Barr* case, there the skilled person also had to subject the radical to a simple test, i.e. expose it to the oxidizing developing agent, and determine if it formed a dye. Under these extremely similar circumstances, it was held that the claim terminology, though functional, met the requirements of 35 U.S.C. 112, second paragraph. The terminology, "anti-inflammatories" should be considered definite for the same reasons as are given in *In re Barr*.

The Examiner's remarks in response to the applicant's position on this issue found at page 6 of the Final Rejection are not understood since the only reasoning given by the Examiner is based on *Genentech*, 108 F.3d at 1366. However, the *Genentech* case related to the first paragraph of 35 U.S.C. 112 (i.e. enabling disclosure) and not to the second paragraph of 35 U.S.C. 112 (i.e. definiteness). Thus, the *Genentech* case is not relevant to whether the claims of the present application meet the requirements of the second paragraph of 35 U.S.C. 112.

Finally, the U.S. Patent Office has issued at least 3112 patents that contain either the term, "anti-inflammatory" or the term, "anti-inflammatories" in the claims. These patents have been examined and are presumed valid pursuant to 35 U.S.C. 282. Thus, in at least 3112 U.S. patents, it was determined that the term, "anti-inflammatories" was sufficiently definite to meet the requirements of 35 U.S.C. 112, second paragraph. The same conclusion should be reached in the present application.

Favorable consideration and withdrawal of the rejection are requested.

F. The Terminology "Compounds Containing Selenium"

Claim 10 has been rejected under 35 U.S.C. §112, second paragraph, on the basis that it contains the phrase, "compounds containing selenium." Although the applicant does not agree

that the Examiner's position is correct, by this amendment, this phrase has been deleted from claim 10 in order to obviate the rejection. Favorable consideration and withdrawal of the rejection in view of this amendment is requested.

Rejections under 35 U.S.C. § 103(a)

Rejection under 35 U.S.C. § 103(a)

Claims 1 through 20 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over U.S. Patent No. 6,162,801, issued to Kita (hereinafter "Kita"), Bissett, D.L. *et al.*, *J. Soc. Cosmet. Chem.* **1992**, *43*, 85-92 (hereinafter "Bissett"), and Darr, D. *et al.*, *British Journal of Dermatology* **1992**, *127*, 247-253 (hereinafter "Darr"), in view of Shimoi, K., *et al.*, *Mutation Research* **1996**, *350*, 153-161 (hereinafter "Shimoi", of which a complete copy is submitted herewith) and U.S. Patent No. 5,776,460, issued to Kim et al. (hereinafter "Kim"). Applicant respectfully traverses this rejection for the reasons set forth below.

Applicant respectfully submits that the Official Action does not set forth a *prima facie* case of obviousness in support of the rejection under 35 U.S.C. § 103(a). According to M.P.E.P. § 2143,

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.
>
> The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. [*Citation omitted.*]

The Official Action cites only one reference, Kita, that sets forth the use of D vitamins to prevent or treat UV-induced damage to the eyes or skin. Kita, however, sets forth the **topical** use of D vitamins, and states that the D vitamins function as a sunscreen. That is, according to Kita, an external layer of vitamin D will protect the eyes or the skin against UV-induced damage at least in part by absorbing the UV radiation before it reaches the body. *See* Kita at col. 4, lines 40-44, and at col. 6, lines 17-20, *inter alia*.

By contrast, Applicant's claimed invention is a method of treating or reducing radiation injury by **orally** administering a composition comprising one or more compounds effective to inhibit at least one of cell differentiation and cell proliferation, for example, a D vitamin, and one or more antioxidants. Kita does not teach or suggest that a D vitamin, be administered **orally** would provide any beneficial effect against UV-induced damage. Moreover, a skilled person reading Kita would not expect oral administration of a D vitamin to provide a beneficial effect against UV-damage because the invention of Kita relies on the D vitamin absorbing the UV radiation to prevent exposure of the skin to the harmful UV radiation. See col. 8, lines 49-54 of Kita. From this clear teaching of Kita, the skilled person would immediately and unequivocally conclude that oral administration of D vitamin would be ineffective since it would not prevent exposure of the skin to harmful UV radiation since the D vitamin would no longer be interposed between the UV radiation and the skin.

On page 7 of the Final Rejection, the Examiner points out that Kita, in summarizing the prior art, mentions that therapeutic vitamin D may be administered orally or by injection. See col. 1, lines 42-44 of Kita. However, the prior art oral administration is not for the purpose of treating radiation injury, but rather, is for the purpose of treating one or more of, "...rickets, osteomalacia, osteoporosis, osteatis, fibrosa, osteosclerosis and other bone diseases, malignant tumors such as breast and colon cancers..." Again, this provides the skilled person with no teaching or suggestion that oral administration of vitamin D would have any beneficial effect in the treatment of radiation injury.

On page 7 of the Final Rejection, the Examiner also takes the position that because Kita teaches that, "In general, the ultraviolet (UV) light absorption spectra of vitamin D and active vitamin D have absorption maxima at 265 nm, with the molar absorption coefficients of about 18900," one of skill in the art would have found it obvious to administer a vitamin D orally in treating radiation injury in a human. The applicant disagrees since if the vitamin D is administered orally, it will be internal to the body. As a result, the vitamin D will not be located between the body or skin and the UV radiation and thus the vitamin D will not be able to prevent exposure to the skin of the harmful UV radiation if taken orally. Also, it does not appear possible for the orally administered vitamin D to absorb UV radiation since the Examiner has not made a showing that the UV radiation would penetrate the skin, muscles bones and internal

organs of a human in order to come into contact with the orally administered vitamin D in order to be absorbed. Skilled persons are aware that the process of absorption required contact between the absorbent and the UV radiation in order to happen. In the case of oral administration of vitamin D, there is no longer any contact between the absorbent, vitamin D, and the UV radiation and thus the vitamin D cannot absorb the UV radiation as is required for it to perform its function according to Kita. See e.g. col. 8, lines 49-54 of Kita.

None of the other references cited by the Examiner teach or suggest that oral administration of vitamin D would provide any beneficial effect in the treatment of radiation injury. Kita cannot provide a reasonable expectation of success for the claimed invention, in view of the arguments given above. As a result, the following elements of a case of *prima facie* obviousness are lacking in the Examiner's rejection:

1. A teaching that oral administration of vitamin D would provide a beneficial effect for treatment of radiation injury, and
2. A teaching to combine vitamin D with an antioxidant.

In the Final Rejection the Examiner also takes the position that,

> "Additionally, oral administrations of vitamin D are well-known in the art. Thus, oral administration of vitamin D would inherently treat radiation injury in a human under the doctrine of inherency."

See page 8 of the Final Rejection. Even if the Examiner's statement is true, MPEP §2141.02 points out that,

> Obviousness cannot be predicated on what is not known at the time an invention is made, even if the inherency of a certain feature is later established. *In re Rijckaert*, 9 F.2d 1531, 28 USPQ2d 1955 (Fed. Cir. 1993).

Thus, since it was not known at the time the present invention was made that vitamin D, ingested orally, would provide any beneficial effect for the treatment of radiation injury, the obviousness rejection based on inherency must fail.

On page 8 of the Final Rejection, the Examiner also took the position that,

> ...since all active composition components herein are known to be useful to treat radiation injury, it is considered *prima facie* obvious to combine them into a single compositions to form a third composition useful for the very same purpose. At least additive therapeutic effects would have been reasonably expected.

There are several problems with this reasoning. First, claims 1-20 of the present application are not directed to a composition. Thus, whether it would have been obvious to make a composition comprising vitamin D and an antioxidant is irrelevant to the patentability of claims 1-20. The key question is whether it would have been obvious to orally administer the composition of the present invention with the expectation of achieving a beneficial effect against radiation injury. See e.g. MPEP §2143 quoted above. The answer to the key question is that it would not be obvious since none of the cited references provides an expectation that oral administration of vitamin D would provide a beneficial effect for treatment of radiation injury.

The second problem with the Examiner's reasoning is that the Examiner has already taken the position that, "...the pharmaceutical art is unpredictable requiring each embodiment to be individually assessed for physiological activity." See page 5, lines 1-2 of the Final Rejection. This statement directly contradicts the Examiner's conclusion that, "At least additive therapeutic effects would have been reasonably expected." The reason for this is that the Examiner has admitted that each embodiment must be individually assessed for physiological activity. As a result, it is not possible to expect a particular therapeutic effect, as the Examiner now claims.

Finally, no skilled person in the pharmaceutical arts would conclude that oral administration of a composition would be effective based on evidence that topical administration is effective. It this were the case, people would be eating sunscreen and rubbing aspirin on their skin with the expectation that these treatments would work. Skilled persons, however, do not extrapolate oral utility from topical utility since it is well known that topical products act in a completely different manner than orally ingested products. Shimoi, cited by the Examiner, for example, was aware that flavonoids exhibited *in vitro* activity as antioxidants and yet conducted experiments to determine whether the same flavonoids would exhibit antioxidant activity *in vivo*, thereby confirming that skilled persons do not conclude from *in vitro* testing that the same activity will be present *in vivo*.

The remaining references cited in the Official Action, that is, Bissett, Darr, Shimoi, and Kim, include descriptions of the use of various antioxidants, or an antioxidant in conjunction with an anti-inflammatory, to treat radiation-induced damage. None of the cited references, however, includes any teaching or suggestion to combine the antioxidants with a compound effective to inhibit at least one of cell differentiation and cell proliferation, nor do any of these references teach or suggest that such a combination should be orally administered for the

treatment of radiation injury. Also, none of these references includes any teaching or suggestion regarding the D vitamins, or oral administration of the D vitamins.

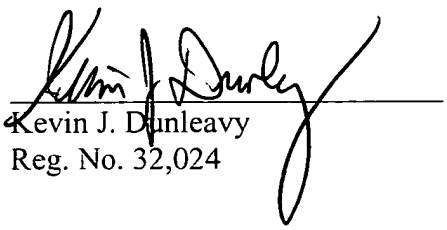
Applicant submits that the cited references do not contain every element of Applicant's claimed invention, as discussed above. Accordingly, Applicant submits that the Official Action does not set forth a *prima facie* case for the obviousness of claim 1 over the cited references.

All of the dependent claims currently pending in the present application ultimately depend from independent claim 1. Applicant respectfully submits that, because independent claim 1 is not obvious over the cited references, dependent claims 2 through 20 are also not obvious. Accordingly, Applicant respectfully requests that the rejection under 35 U.S.C. § 103(a) be withdrawn upon reconsideration.

Conclusion

In view of the foregoing amendments and remarks, Applicant respectfully submits that all of the pending claims are in condition for allowance and respectfully requests a favorable Office Action so indicating.

Respectfully submitted,



Kevin J. Dunleavy
Reg. No. 32,024

Dated: August 26, 2003

KNOBLE & YOSHIDA LLC
Eight Penn Center, Suite 1350
1628 John F. Kennedy, Jr. Blvd.
Philadelphia, PA 19103
(215) 599-0600
Customer No. 21,302